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=> d his full

     FILE 'HCAPLUS' ENTERED AT 12:42:15 ON 18 DEC 2002
L1           47 SEA ABB=ON  (?HEMATOPOIETIC? OR ?ENDOTHELIAL?)(W)?PROGENIT?(W)C
                ELL(W)GROWTH
L2           48 SEA ABB=ON  L1 OR ?ANTI?(W)?TUMORIG?(W)?TREAT?
L3           74 SEA ABB=ON  (?RESTENOS? OR ?FIBROT?(W)(BUILDUP OR BUILD(W)UP)(W
                )?PREVENT?) AND (?PROSTHET?(W)?IMPLANT?)
L4          121 SEA ABB=ON  L2 OR L3
L5          680 SEA ABB=ON  P(2A)ANTIGEN(3A)?CELL?(W)?ABNORM?(W)?PROLIF? OR
                ?POLYCYTHEM?(W)?VERA?
L6          799 SEA ABB=ON  L4 OR L5
L7            0 SEA ABB=ON  B19(3A)?PARVOVIRUS?(W)VP2(W)(?CAPSID? OR ?VIRION?)(
                W)(?PARTICLE? OR ?FRAGMENT?)
L8            2 SEA ABB=ON  B19(3A)?PARVOVIRUS?(W)VP2(W)(?CAPSID? OR ?VIRION?)

L9            8 SEA ABB=ON  B19(3A)?PARVOVIRUS?(W)VP2
L10         436 SEA ABB=ON  B19(3A)?PARVOVIRUS?
L11           1 SEA ABB=ON  L6 AND L10
                D AU
L12        3662 SEA ABB=ON  (?HEMATOPOIETIC? OR ?ENDOTHELIAL?)(W)?PROGENIT?
L13        3663 SEA ABB=ON  L12 OR ?ANTI?(W)?TUMORIG?(W)?TREAT?
L14        4397 SEA ABB=ON  L13 OR L3 OR L5
L15           0 SEA ABB=ON  L14 AND B19(3A)?PARVOVIRUS?(W)VP2(W)(?CAPSID? OR
                ?VIRION?)(W)(?PARTICLE? OR ?FRAGMENT?)
L16           0 SEA ABB=ON  L14 AND B19(3A)?PARVOVIRUS?(W)VP2(W)(?CAPSID? OR
                ?VIRION?)
L17           0 SEA ABB=ON  L14 AND B19(3A)?PARVOVIRUS?(W)VP2
L18           5 SEA ABB=ON  L14 AND B19(3A)?PARVOVIRUS?
                D TI 1-5
L19           5 SEA ABB=ON  L14 AND B19(3A)?PARVOVIR?
                D AU 1-5
L20           0 SEA ABB=ON  L19 AND (GLU(W)GLU(W)TYR OR ?GLUTAMIN?(W)?GLUTAMIN?
                (W)?TYROSIN?)

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO' ENTERED AT
     12:59:57 ON 18 DEC 2002
L21          38 SEA ABB=ON  L19
L22          19 DUP REMOV L21 (19 DUPLICATES REMOVED)
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retrieved only 1 cit, inventor's work, for Allen
so I broadened the search statements somewhat, until

5 cits were retrieved - see attached

19 cits from other databases.

=> d ibib abs 1

L3 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:368128 HCAPLUS
DOCUMENT NUMBER: 133:9083
TITLE: Use of parvovirus capsid particles in the inhibition of cell proliferation and migration
INVENTOR(S): **Broliden, Kristina; Westgren, Magnus**
PATENT ASSIGNEE(S): Tripep AB, Swed.
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000030668	A2	20000602	WO 1999-IB2112	19991123
WO 2000030668	A3	20001109		
W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
SE 9804022	A	20000525	SE 1998-4022	19981124
EP 1131085	A2	20010912	EP 1999-968407	19991123
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NO 2001002534	A	20010629	NO 2001-2534	20010523

PRIORITY APPLN. INFO.: SE 1998-4022 A 19981124
WO 1999-IB2112 W 19991123

AB The invention described herein relates to the discovery of methods and compns. for the inhibition of growth and/or migration of cells that have the P antigen, including but not limited to, cells of hematopoietic origin and endothelial cells. More specifically, parvovirus capsid particles or fragments of parvovirus capsid proteins are used to manuf. medicaments that can be administered to a subject to inhibit hematopoietic progenitor cell growth (e.g., prior to stem cell transplantation), endothelial cell growth, (e.g., as an anti-tumorigenesis treatment or to prevent restenosis or fibrotic build up following prosthetic implantation), or to prevent disorders that involve the abnormal proliferation of cells that have the P antigen (e.g., polycythemia vera).

=> d ind 1

L3 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2002 ACS
IC ICM A61K038-00
CC 63-5 (Pharmaceuticals)
ST parvovirus capsid inhibitor cell migration proliferation
IT Antigens
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(P; use of parvovirus capsid particles in the inhibition of cell proliferation and migration)
IT Virion structure
(capsid; use of parvovirus capsid particles in the inhibition of cell proliferation and migration)
IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(capsid; use of parvovirus capsid particles in the inhibition of cell proliferation and migration)
IT Prosthetic materials and Prosthetics
(endothelial cell ingrowth into; use of parvovirus capsid particles in the inhibition of cell proliferation and migration)
IT Blood vessel
(endothelium, inhibition of growth and migration of; use of parvovirus capsid particles in the inhibition of cell proliferation and migration)
IT Embryo, animal
(fetus, treatment of; use of parvovirus capsid particles in the inhibition of cell proliferation and migration)
IT Cell
(stem, transplant; use of parvovirus capsid particles in the inhibition of cell proliferation and migration)
IT Angiogenesis inhibitors
B19 virus
Cell migration
Cell proliferation
Drug delivery systems
Hematopoiesis
Transformation, neoplastic
(use of parvovirus capsid particles in the inhibition of cell proliferation and migration)

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=> d que stat l19
L3          74 SEA FILE=HCAPLUS ABB=ON  (?RESTENOS? OR ?FIBROT?(W)(BUILDUP OR
               BUILD(W)UP)(W)?PREVENT?) AND (?PROSTHET?(W)?IMPLANT?)
L5         680 SEA FILE=HCAPLUS ABB=ON  P(2A)ANTIGEN(3A)?CELL?(W)?ABNORM?(W)?P
               ROLIF? OR ?POLYCYTHEM?(W)?VERA?
L12       3662 SEA FILE=HCAPLUS ABB=ON  (?HEMATOPOIETIC? OR ?ENDOTHELIAL?)(W)?
               PROGENIT?
L13       3663 SEA FILE=HCAPLUS ABB=ON  L12 OR ?ANTI?(W)?TUMORIG?(W)?TREAT?
L14       4397 SEA FILE=HCAPLUS ABB=ON  L13 OR L3 OR L5
L19          5 SEA FILE=HCAPLUS ABB=ON  L14 AND B19(3A)?PARVOVIR?


=> d ibib abs 1-5 l19

L19  ANSWER 1 OF 5  HCAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         2000:368128  HCAPLUS
DOCUMENT NUMBER:          133:9083
TITLE:                    Use of parvovirus capsid particles in the inhibition
                          of cell proliferation and migration
INVENTOR(S):              Broliden, Kristina; Westgren, Magnus
PATENT ASSIGNEE(S):       Tripep AB, Swed.
SOURCE:                   PCT Int. Appl., 39 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
     WO 2000030668      A2   20000602      WO 1999-IB2112   19991123
     WO 2000030668      A3   20001109
         W:  AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,
             CU, CZ, CZ, DE, DE, DK, DK, DM, EE, EE, ES, FI, FI, GB, GD, GE,
             GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL,
             PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA,
             UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
             DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
             CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     SE 9804022         A    20000525      SE 1998-4022     19981124
     EP 1131085         A2   20010912      EP 1999-968407   19991123
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
     NO 2001002534      A    20010629      NO 2001-2534     20010523
PRIORITY APPLN. INFO.:                   SE 1998-4022     A  19981124
                                         WO 1999-IB2112   W  19991123
AB   The invention described herein relates to the discovery of methods and
     compns. for the inhibition of growth and/or migration of cells that have
     the P antigen, including but not limited to, cells of hematopoietic origin
     and endothelial cells.  More specifically, parvovirus capsid particles or
     fragments of parvovirus capsid proteins are used to manuf. medicaments
     that can be administered to a subject to inhibit hematopoietic
     progenitor cell growth (e.g., prior to stem cell transplantation),
     endothelial cell growth, (e.g., as an anti-tumorigenesis
     treatment or to prevent restenosis or fibrotic build up
     following prosthetic implantation), or to prevent
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disorders that involve the abnormal proliferation of cells that have the P antigen (e.g., **polycythemia vera**).

L19 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:74623 HCAPLUS
DOCUMENT NUMBER: 132:288736
TITLE: Adeno-associated virus 2-mediated transduction and erythroid lineage-restricted expression from parvovirus B19p6 promoter in primary human **hematopoietic progenitor** cells
AUTHOR(S): Kurpad, Chandrika; Mukherjee, Pinku; Wang, Xu-Shan; Ponnazhagan, Selvarangan; Li, Linglin; Yoder, Mervin C.; Srivastava, Arun
CORPORATE SOURCE: Department of Microbiology & Immunology, Indiana University School of Medicine, Indianapolis, IN, 46202, USA
SOURCE: Journal of Hematotherapy & Stem Cell Research (1999), 8(6), 585-592
CODEN: JHERFM; ISSN: 1525-8165
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Human **parvovirus B19** gene expression from the viral p6 promoter (B19p6) is restricted to primary human hematopoietic cells undergoing erythroid differentiation. We have demonstrated that expression from this promoter does not occur in established human erythroid cell lines in the context of a recombinant parvovirus genome (Ponnazhagan et al. J Virol 69:8096-8101, 1995). However, abundant expression from this promoter can be readily detected in primary human bone marrow cells (Wang et al. Proc Natl Acad Sci USA 92:12416-12420, 1995; Ponnazhagan et al. J Gen Virol 77:1111-1122, 1996). In the present studies, we investigated the pattern of expression from the B19p6 promoter in primary human bone marrow-derived CD34+ HPC undergoing differentiation into myeloid and erythroid lineages. CD34+ cells were transduced with recombinant adeno-assocd. virus 2 (AAV) vectors contg. the .beta.-galactosidase (lacZ) gene under the control of the following promoters/enhancers: the cytomegalovirus promoter (vCMVp-lacZ), B19p6 promoter (vB19p6-lacZ), B19p6 promoter with an upstream erythroid cell-specific enhancer element (HS-2) from the locus control region (LCR) from the human .beta.-globin gene cluster (vHS2-B19p6-lacZ), and the human .beta.-globin gene promoter with the HS-2 enhancer (vHS2-.beta.p-lacZ). Transgene expression was evaluated either 48 h after infection or following erythroid differentiation in vitro for 3 wk. Whereas high-level expression from the CMV promoter 48 h after infection diminished with time, low-level expression from the B19p6 and the .beta.-globin promoters increased significantly following erythroid differentiation. Furthermore, in HPC assays, there was no significant difference in the level of expression from the CMV promoter in myeloid or erythroid cell-derived colonies. Expression from the B19p6 and the .beta.-globin promoters, on the other hand, was restricted to erythroid cell colonies. These data further corroborate that the B19p6 promoter is erythroid cell-specific and suggest that the recombinant AAV-B19 hybrid vectors may prove useful in gene therapy of human hemoglobinopathies in general and sickle cell anemia and .beta.-thalassemia in particular.
REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:303214 HCAPLUS
DOCUMENT NUMBER: 129:77199
TITLE: Recombinant human **parvovirus B19** vectors: erythroid cell-specific delivery and expression of transduced genes
AUTHOR(S): Ponnazhagan, Selvarangan; Weigel, Kirsten A.; Raikwar, Sudhanshu P.; Mukherjee, Pinku; Yoder, Mervin C.; Srivastava, Arun
CORPORATE SOURCE: Department of Microbiology & Immunology, Indiana University School of Medicine, Indianapolis, IN, 46202, USA
SOURCE: Journal of Virology (1998), 72(6), 5224-5230
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A novel packaging strategy combining the salient features of two human parvoviruses, namely the pathogenic **parvovirus B19** and the nonpathogenic adeno-assocd. virus type 2 (AAV), was developed to achieve erythroid cell-specific delivery as well as expression of the transduced gene. The development of such a chimeric vector system was accomplished by packaging heterologous DNA sequences cloned within the inverted terminal repeats of AAV and subsequently packaging the DNA inside the capsid structure of B19 virus. Recombinant B19 virus particles were assembled, as evidenced by electron microscopy as well as DNA slot blot analyses. The hybrid vector failed to transduce nonerythroid human cells, such as 293 cells, as expected. However, MB-02 cells, a human megakaryocytic leukemia cell line which can be infected by B19 virus following erythroid differentiation with erythropoietin, were readily transduced by this vector. The hybrid vector was also found to specifically target the erythroid population in primary human bone marrow cells as well as more immature **hematopoietic progenitor** cells following erythroid differentiation, as evidenced by selective expression of the transduced gene in these target cells. Preincubation with anticapsid antibodies against B19 virus, but not anticapsid antibodies against AAV, inhibited transduction of primary human erythroid cells. The efficiency of transduction of primary human erythroid cells by the recombinant B19 virus vector was significantly higher than that by the recombinant AAV vector. Further development of the AAV-B19 virus hybrid vector system should prove beneficial in gene therapy protocols aimed at the correction of inherited and acquired human diseases affecting cells of erythroid lineage.

L19 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:13970 HCAPLUS
DOCUMENT NUMBER: 124:111870
TITLE: **Parvovirus B19** promoter at map unit 6 confers autonomous replication competence and erythroid specificity to adeno-associated virus 2 in primary human **hematopoietic progenitor** cells
AUTHOR(S): Wang, Xu-Shan; Yoder, Mervin C.; Zhou, Shang Zhen; Srivastava, Arun
CORPORATE SOURCE: Dep. Med., Indiana Univ. Sch. Med., Indianapolis, IN, 46202, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1995), 92(26), 12416-20
CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The pathogenic human **parvovirus B19** is an autonomously replicating virus with a remarkable tropism for human erythroid progenitor cells. Although the target cell specificity for B19 infection has been suggested to be mediated by the erythrocyte P-antigen receptor (globoside), a no. of nonerythroid cells that express this receptor are nonpermissive for B19 replication. To directly test the role of expression from the B19 promoter at map unit 6 (B19p6) in the erythroid cell specificity of B19, we constructed a recombinant adeno-assocd. virus 2 (AAV), in which the authentic AAV promoter at map unit 5 (AAVp5) was replaced by the B19p6 promoter. Although the wild-type (wt) AAV requires a helper virus for its optimal replication, we hypothesized that inserting the B19p6 promoter in a recombinant AAV would permit autonomous viral replication, but only in erythroid progenitor cells. In this report, we provide evidence that the B19p6 promoter is necessary and sufficient to impart autonomous replication competence and erythroid specificity to AAV in primary human **hematopoietic progenitor** cells. Thus, expression from the B19p6 promoter plays an important role in post-P-antigen receptor erythroid-cell specificity of **parvovirus B19**. The AAV-B19 hybrid vector system may also prove to be useful in potential gene therapy of human hemoglobinopathies.

L19 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:262990 HCAPLUS
DOCUMENT NUMBER: 120:262990
TITLE: Adeno-associated virus 2-mediated high efficiency gene transfer into immature and mature subsets of **hematopoietic progenitor** cells in human umbilical cord blood
AUTHOR(S): Zhou, Shang Zhen; Cooper, Scott; Kang, Li Ya; Ruggieri, Luciano; Heimfeld, Shelly; Srivastava, Arun; Broxmeyer, Hal E.
CORPORATE SOURCE: Sch. Med., Indiana Univ., Indianapolis, IN, 46202-5120, USA
SOURCE: Journal of Experimental Medicine (1994), 179(6), 1867-75
CODEN: JEMEAV; ISSN: 0022-1007
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Recombinant adeno-assocd. virus 2 (AAV) virions were constructed contg. a gene for resistance to neomycin (neoR), under the control of either the herpesvirus thymidine kinase (TK) gene promoter (vTK-Neo), or the human **parvovirus B19** p6 promoter (vB19-Neo), as well as those contg. an upstream erythroid cell-specific enhancer (HS-2) from the locus control region of the human .beta.-globin gene cluster (vHS2-TK-Neo; vHS2-B19-Neo). These recombinant virions were used to infect either low d. or highly enriched populations of CD34+ cells isolated from human umbilical cord blood. In clonogenic assays initiated with cells infected with the different recombinant AAV-Neo virions, equiv. high freq. transduction of the neoR gene into slow-cycling multipotential, erythroid, and granulocyte/macrophage (GM) progenitor cells, including those with high proliferative potential, was obtained without pre-stimulation with growth factors, indicating that these immature and mature **hematopoietic progenitor** cells were susceptible to infection by the recombinant AAV virions. Successful transduction did not require and was not enhanced by pre-stimulation of these cell populations

with cytokines. The functional activity of the transduced neo gene was evident by the development of resistance to the drug G418, a neomycin analog. Individual high and low proliferative colony-forming unit (CFU)-GM, burst-forming unit-erythroid, and CFU-granulocyte erythroid macrophage megakaryocyte colonies from mock-infected, or the recombinant virus-infected cultures were subjected to polymerase chain reaction anal. using a neo-specific synthetic oligonucleotide primer pair. A 276-bp DNA fragment that hybridized with a neo-specific DNA probe on Southern blots was only detected in those colonies cloned from the recombinant virus-infected cells, indicating stable integration of the transduced neo gene. These studies suggest that at parvovirus-based vectors may prove to be a useful alternative to the more commonly used retroviral vectors for high efficiency gene transfer into slow or noncycling primitive **hematopoietic progenitor** cells, without the need for growth factor stimulation, which could potentially led to differentiation of these cells before transplantation.

```
=> d que stat l22
L3            74 SEA FILE=HCAPLUS ABB=ON  (?RESTENOS? OR ?FIBROT?(W)(BUILDUP OR
                 BUILD(W)UP)(W)?PREVENT?) AND (?PROSTHET?(W)?IMPLANT?)
L5           680 SEA FILE=HCAPLUS ABB=ON  P(2A)ANTIGEN(3A)?CELL?(W)?ABNORM?(W)?P
                 ROLIF? OR ?POLYCYTHEM?(W)?VERA?
L12         3662 SEA FILE=HCAPLUS ABB=ON  (?HEMATOPOIETIC? OR ?ENDOTHELIAL?)(W)?
                 PROGENIT?
L13         3663 SEA FILE=HCAPLUS ABB=ON  L12 OR ?ANTI?(W)?TUMORIG?(W)?TREAT?
L14         4397 SEA FILE=HCAPLUS ABB=ON  L13 OR L3 OR L5
L19            5 SEA FILE=HCAPLUS ABB=ON  L14 AND B19(3A)?PARVOVIR?
L21           38 SEA L19
L22           19 DUP REMOV L21 (19 DUPLICATES REMOVED)
=> d l22 ibib abs 1-19

L22  ANSWER 1 OF 19     MEDLINE
ACCESSION NUMBER:    2002186852     MEDLINE
DOCUMENT NUMBER:     21916087   PubMed ID: 11921028
TITLE:               Anemia following human parvovirus B19
                     infection in a patient with polycythemia
                     vera.
AUTHOR:              Kaptan Kursad; Beyan Cengiz; Cetin Turker; Ural Ali Ugur;
                     Ustun Celalettin; Avcu Ferit; Nevruz Oral; Guney Cakir;
                     Kubar Ayhan
SOURCE:              AMERICAN JOURNAL OF HEMATOLOGY, (2002 Apr) 69 (4) 296-7.
                     Journal code: 7610369. ISSN: 0361-8609.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       Letter
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         200205
ENTRY DATE:          Entered STN: 20020403
                     Last Updated on STN: 20020514
                     Entered Medline: 20020513

L22  ANSWER 2 OF 19  BIOSIS  COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
     1
ACCESSION NUMBER:    2002:281430  BIOSIS
DOCUMENT NUMBER:     PREV200200281430
TITLE:               Anemia following human parvovirus B19
```

infection in a patient with **polycythemia vera**.
AUTHOR(S): Kaptan, Kursad (1); Beyan, Cengiz (1); Cetin, Turker (1); Ural, Ali Ugur (1); Ustun, Celalettin (1); Avcu, Ferit (1); Nevruz, Oral (1); Yalcin, Atilla (1); Guney, Cakir; Kubar, Ayhan
CORPORATE SOURCE: (1) Hematology Department, Gulhane Military Medical Academy, Etlik, Ankara Turkey
SOURCE: American Journal of Hematology, (April, 2002) Vol. 69, No. 4, pp. 296-297. http://www.interscience.wiley.com. print. ISSN: 0361-8609.
DOCUMENT TYPE: Article; Letter
LANGUAGE: English

L22 ANSWER 3 OF 19 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:288158 BIOSIS
DOCUMENT NUMBER: PREV200100288158
TITLE: Pathogenesis of anemia during human immunodeficiency virus infection.
AUTHOR(S): Semba, Richard D. (1); Gray, Glenda E.
CORPORATE SOURCE: (1) 550 North Broadway, Suite 700, Baltimore, MD, 21205: rdsemba@jhmi.edu USA
SOURCE: Journal of Investigative Medicine, (May, 2001) Vol. 49, No. 3, pp. 225-239. print. ISSN: 1081-5589.
DOCUMENT TYPE: General Review
LANGUAGE: English
SUMMARY LANGUAGE: English

L22 ANSWER 4 OF 19 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2001112569 MEDLINE
DOCUMENT NUMBER: 20574421 PubMed ID: 11125248
TITLE: Recombinant **parvovirus B19** empty capsids inhibit fetal hematopoietic colony formation in vitro.
AUTHOR: Lindton B; Tolfvenstam T; Norbeck O; Markling L; Ringden O; Westgren M; Broliden K
CORPORATE SOURCE: Department of Obstetrics and Gynecology, Karolinska Institute, Huddinge University Hospital, Huddinge, Sweden.
SOURCE: FETAL DIAGNOSIS AND THERAPY, (2001 Jan-Feb) 16 (1) 26-31. Journal code: 9107463. ISSN: 1015-3837.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010208

AB Erythroid lineage cells are target cells for human **parvovirus B19**, and a natural infection often results in transient anemia. To determine whether recombinant B19 capsid proteins (VP1/VP2) also inhibit human **hematopoietic progenitor** growth, a model system was set up. The B19 capsids were inoculated into primary cultures of hematopoietic stem cells derived from human fetal liver, resulting in a 70-95% reduction of BFU-E (burst-forming unit erythroid cells) as compared with the medium control. A similar effect was seen in human hematopoietic stem cell cultures derived from cord blood and adult bone marrow.

Preincubation of the B19 capsids with either a monoclonal antibody to the virus or with B19 IgG positive human sera reduced the inhibitory effect. Furthermore, the inhibitory effect could be reduced by preincubating the target cells with a monoclonal antibody to the cellular receptor for the virus, the P antigen. These findings thus show that the inhibition of colony formation of human hematopoietic stem cells can occur in the absence of **parvovirus B19** nonstructural proteins. We speculate that B19 capsid could provide a possible strategy to downregulate indigenous hematopoiesis in fetal stem cell transplantations. Copyright 2001 S. Karger AG, Basel

L22 ANSWER 5 OF 19 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2000-399928 [34] WPIDS
DOC. NO. CPI: C2000-120757
TITLE: Use of empty non-infectious recombinant **B19** **parvovirus** capsids, **B19** capsid proteins or fragments of B19 capsid proteins for the production of a medicament for the inhibition of growth or migration of cells containing the P antigen.
DERWENT CLASS: B04 D16
INVENTOR(S): BROLIDEN, K; WESTGREN, M
PATENT ASSIGNEE(S): (BROL-I) BROLIDEN K; (WEST-I) WESTGREN M; (TRIP-N) TRIPEP AB
COUNTRY COUNT: 90
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000030668	A2	20000602	(200034)*	EN	39
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW					
SE 9804022	A	20000525	(200036)		
AU 2000025666	A	20000613	(200043)		
NO 2001002534	A	20010629	(200147)		
EP 1131085	A2	20010912	(200155)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
CZ 2001001369	A3	20011017	(200172)		
KR 2001080518	A	20010822	(200213)		
CN 1328469	A	20011226	(200227)		
HU 2001004298	A2	20020328	(200234)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000030668	A2	WO 1999-IB2112	19991123
SE 9804022	A	SE 1998-4022	19981124
AU 2000025666	A	AU 2000-25666	19991123
NO 2001002534	A	WO 1999-IB2112	19991123
		NO 2001-2534	20010523
EP 1131085	A2	EP 1999-968407	19991123
		WO 1999-IB2112	19991123
CZ 2001001369	A3	WO 1999-IB2112	19991123

		CZ 2001-1369	19991123
KR 2001080518	A	KR 2001-706374	20010521
CN 1328469	A	CN 1999-813653	19991123
HU 2001004298	A2	WO 1999-IB2112	19991123
		HU 2001-4298	19991123

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000025666	A	Based on	WO 200030668
EP 1131085	A2	Based on	WO 200030668
CZ 2001001369	A3	Based on	WO 200030668
HU 2001004298	A2	Based on	WO 200030668

PRIORITY APPLN. INFO: SE 1998-4022 19981124
AN 2000-399928 [34] WPIDS
AB WO 200030668 A UPAB: 20000718
NOVELTY - Empty, non-infectious, recombinant **B19** **parvovirus** capsids, **B19** capsid proteins or fragments of B19 capsid proteins for the production of a medicament for the inhibition of growth or migration of cells that have the P antigen.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) inhibiting the growth or migration of a cell having the P antigen comprising contacting the cell with a capsid agent either **B19** **parvovirus** capsid, **B19** capsid protein or a fragment of a B19 capsid protein and measuring the inhibition of cell growth or cell migration; and

(2) a kit comprising a capsid agent either **B19** **parvovirus** capsid, **B19** capsid protein or a fragment of a B19 capsid protein for administration to a subject for hematopoetic progenitor cell growth inhibition, endothelial cell growth inhibition or treatment of a hematological proliferative.

USE - For inhibition of hematopoietic cell growth, endothelial cell growth or endothelial migration. For treatment of a subject, especially a fetus, prior to stem cell transplantation. For the treatment of angiogenesis, tumorigenesis, endothelial cell ingrowth into an implanted prosthetic device or hematological proliferative disorders (claimed) e.g. **polycythemia vera**.

ADVANTAGE - The **B19 parvovirus** capsid provides treatment for diseases such as polycythemia for which there are no current specific pharmalogical treatment and for which median survival time without treatment is short.

Dwg.0/8

L22 ANSWER 6 OF 19 MEDLINE
ACCESSION NUMBER: 2000108360 MEDLINE
DOCUMENT NUMBER: 20108360 PubMed ID: 10645762
TITLE: Gene delivery to human **hematopoietic** **progenitor** cells to address inherited defects in the erythroid cellular lineage.
COMMENT: Comment on: J Hematother Stem Cell Res. 1999 Dec;8(6):585-92
Comment on: J Hematother Stem Cell Res. 1999 Dec;8(6):593-600
AUTHOR: Strayer D S
SOURCE: J Hematother Stem Cell Res, (1999 Dec) 8 (6) 573-4.

Journal code: 100892915. ISSN: 1525-8165.
PUB. COUNTRY: United States
DOCUMENT TYPE: Commentary
Editorial
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 20000229
Last Updated on STN: 20000229
Entered Medline: 20000214

L22 ANSWER 7 OF 19 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2000108363 MEDLINE
DOCUMENT NUMBER: 20108363 PubMed ID: 10645765
TITLE: Adeno-associated virus 2-mediated transduction and erythroid lineage-restricted expression from parvovirus B19p6 promoter in primary human **hematopoietic progenitor** cells.
COMMENT: Comment in: J Hematother Stem Cell Res. 1999 Dec;8(6):573-4
AUTHOR: Kurpad C; Mukherjee P; Wang X S; Ponnazhagan S; Li L; Yoder M C; Srivastava A
CORPORATE SOURCE: Department of Microbiology & Immunology, Walther Oncology Center, Indiana University School of Medicine, Indianapolis 46202-5120, USA.
CONTRACT NUMBER: HL-48342 (NHLBI)
HL-53586 (NHLBI)
HL-58881 (NHLBI)
+
SOURCE: J Hematother Stem Cell Res, (1999 Dec) 8 (6) 585-92.
Journal code: 100892915. ISSN: 1525-8165.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 20000229
Last Updated on STN: 20000229
Entered Medline: 20000214

AB Human **parvovirus B19** gene expression from the viral p6 promoter (B19p6) is restricted to primary human hematopoietic cells undergoing erythroid differentiation. We have demonstrated that expression from this promoter does not occur in established human erythroid cell lines in the context of a recombinant parvovirus genome (Ponnazhagan et al. J Virol 69:8096-8101, 1995). However, abundant expression from this promoter can be readily detected in primary human bone marrow cells (Wang et al. Proc Natl Acad Sci USA 92:12416-12420, 1995; Ponnazhagan et al. J Gen Virol 77:1111-1122, 1996). In the present studies, we investigated the pattern of expression from the B19p6 promoter in primary human bone marrow-derived CD34+ HPC undergoing differentiation into myeloid and erythroid lineages. CD34+ cells were transduced with recombinant adeno-associated virus 2 (AAV) vectors containing the beta-galactosidase (lacZ) gene under the control of the following promoters/enhancers: the cytomegalovirus promoter (vCMVp-lacZ), B19p6 promoter (vB19p6-lacZ), B19p6 promoter with an upstream erythroid cell-specific enhancer element (HS-2) from the locus control region (LCR) from the human beta-globin gene cluster (vHS2-B19p6-lacZ), and the human beta-globin gene promoter with the HS-2 enhancer (vHS2-beta p-lacZ). Transgene expression was evaluated either 48 h after infection or following erythroid differentiation in

vitro for 3 weeks. Whereas high-level expression from the CMV promoter 48 h after infection diminished with time, low-level expression from the B19p6 and the beta-globin promoters increased significantly following erythroid differentiation. Furthermore, in HPC assays, there was no significant difference in the level of expression from the CMV promoter in myeloid or erythroid cell-derived colonies. Expression from the B19p6 and the beta-globin promoters, on the other hand, was restricted to erythroid cell colonies. These data further corroborate that the B19p6 promoter is erythroid cell-specific and suggest that the recombinant AAV-B19 hybrid vectors may prove useful in gene therapy of human hemoglobinopathies in general and sickle cell anemia and beta-thalassemia in particular.

L22 ANSWER 8 OF 19 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 1998241766 MEDLINE
DOCUMENT NUMBER: 98241766 PubMed ID: 9573295
TITLE: Recombinant human **parvovirus B19** vectors: erythroid cell-specific delivery and expression of transduced genes.
AUTHOR: Ponnazhagan S; Weigel K A; Raikwar S P; Mukherjee P; Yoder M C; Srivastava A
CORPORATE SOURCE: Department of Microbiology & Immunology, Indiana University School of Medicine, Indianapolis, Indiana 46202, USA.
CONTRACT NUMBER: HL-48342 (NHLBI)
HL-53586 (NHLBI)
HL-58881 (NHLBI)
+
SOURCE: JOURNAL OF VIROLOGY, (1998 Jun) 72 (6) 5224-30.
Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199805
ENTRY DATE: Entered STN: 19980609
Last Updated on STN: 19980609
Entered Medline: 19980527

AB A novel packaging strategy combining the salient features of two human parvoviruses, namely the pathogenic **parvovirus B19** and the nonpathogenic adeno-associated virus type 2 (AAV), was developed to achieve erythroid cell-specific delivery as well as expression of the transduced gene. The development of such a chimeric vector system was accomplished by packaging heterologous DNA sequences cloned within the inverted terminal repeats of AAV and subsequently packaging the DNA inside the capsid structure of B19 virus. Recombinant B19 virus particles were assembled, as evidenced by electron microscopy as well as DNA slot blot analyses. The hybrid vector failed to transduce nonerythroid human cells, such as 293 cells, as expected. However, MB-02 cells, a human megakaryocytic leukemia cell line which can be infected by B19 virus following erythroid differentiation with erythropoietin (N. C. Munshi, S. Z. Zhou, M. J. Woody, D. A. Morgan, and A. Srivastava, J. Virol. 67:562-566, 1993) but lacks the putative receptor for AAV (S. Ponnazhagan, X.-S. Wang, M. J. Woody, F. Luo, L. Y. Kang, M. L. Nallari, N. C. Munshi, S. Z. Zhou, and A. Srivastava, J. Gen. Virol. 77:1111-1122, 1996), were readily transduced by this vector. The hybrid vector was also found to specifically target the erythroid population in primary human bone marrow cells as well as more immature **hematopoietic progenitor** cells following erythroid differentiation, as evidenced by selective expression of the transduced gene in these target cells. Preincubation

with anticapsid antibodies against B19 virus, but not anticapsid antibodies against AAV, inhibited transduction of primary human erythroid cells. The efficiency of transduction of primary human erythroid cells by the recombinant B19 virus vector was significantly higher than that by the recombinant AAV vector. Further development of the AAV-B19 virus hybrid vector system should prove beneficial in gene therapy protocols aimed at the correction of inherited and acquired human diseases affecting cells of erythroid lineage.

L22 ANSWER 9 OF 19 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:68983 BIOSIS
DOCUMENT NUMBER: PREV199800068983
TITLE: Development of human **parvovirus B19** vectors: Erythroid cell-specific delivery and expression of transduced genes.
AUTHOR(S): Ponnazhagan, S.; Mukherjee, P.; Yoder, M. C.; Srivastava, A.
CORPORATE SOURCE: Indiana Univ. Sch. Med., Indianapolis, IN USA
SOURCE: Blood, (Nov. 15, 1997) Vol. 90, No. 10 SUPPL. 1 PART 1, pp. 602A.
Meeting Info.: 39th Annual Meeting of the American Society of Hematology San Diego, California, USA December 5-9, 1997 The American Society of Hematology
. ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English

L22 ANSWER 10 OF 19 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:61250 BIOSIS
DOCUMENT NUMBER: PREV199800061250
TITLE: **Parvovirus B19** NS-1 gene is embryonic-lethal in transgenic mice.
AUTHOR(S): Wang, X.-S.; Srivastava, A.
CORPORATE SOURCE: Indiana Univ. Sch. Med., Indianapolis, IN USA
SOURCE: Blood, (Nov. 15, 1997) Vol. 90, No. 10 SUPPL. 1 PART 2, pp. 157B.
Meeting Info.: Thirty-ninth Annual Meeting of the American Society of Hematology San Diego, California, USA December 5-9, 1997 The American Society of Hematology
. ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English

L22 ANSWER 11 OF 19 MEDLINE
ACCESSION NUMBER: 96386498 MEDLINE
DOCUMENT NUMBER: 96386498 PubMed ID: 8794248
TITLE: Adeno-associated virus 2-mediated transduction and erythroid lineage-specific expression in human **hematopoietic progenitor** cells.
AUTHOR: Srivastava A; Wang X S; Ponnazhagan S; Zhou S Z; Yoder M C
CORPORATE SOURCE: Division of Hematology and Oncology, Department of Medicine, Indiana University School of Medicine, Indianapolis 46202-5120, USA.
CONTRACT NUMBER: AI-26323 (NIAID)
DK-49218 (NIDDK)
HL-48342 (NHLBI)
+
SOURCE: CURRENT TOPICS IN MICROBIOLOGY AND IMMUNOLOGY, (1996) 218

93-117. Ref: 72
Journal code: 0110513. ISSN: 0070-217X.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199610
ENTRY DATE: Entered STN: 19961219
Last Updated on STN: 19961219
Entered Medline: 19961029

L22 ANSWER 12 OF 19 MEDLINE DUPLICATE 5

ACCESSION NUMBER: 96109277 MEDLINE
DOCUMENT NUMBER: 96109277 PubMed ID: 8618912

TITLE: **Parvovirus B19** promoter at map unit 6 confers autonomous replication competence and erythroid specificity to adeno-associated virus 2 in primary human **hematopoietic progenitor** cells.

AUTHOR: Wang X S; Yoder M C; Zhou S Z; Srivastava A
CORPORATE SOURCE: Department of Medicine, Indiana University School of Medicine, Indianapolis 46202, USA.

CONTRACT NUMBER: AI-26323 (NIAID)
HL-48342 (NHLBI)
HL-53586 (NHLBI)
+
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1995 Dec 19) 92 (26) 12416-20.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199606
ENTRY DATE: Entered STN: 19960620
Last Updated on STN: 19970203
Entered Medline: 19960607

AB The pathogenic human **parvovirus B19** is an autonomously replicating virus with a remarkable tropism for human erythroid progenitor cells. Although the target cell specificity for B19 infection has been suggested to be mediated by the erythrocyte P-antigen receptor (globoside), a number of nonerythroid cells that express this receptor are nonpermissive for B19 replication. To directly test the role of expression from the B19 promoter at map unit 6 (B19p6) in the erythroid cell specificity of B19, we constructed a recombinant adeno-associated virus 2 (AAV), in which the authentic AAV promoter at map unit 5 (AAVp5) was replaced by the B19p6 promoter. Although the wild-type (wt) AAV requires a helper virus for its optimal replication, we hypothesized that inserting the B19p6 promoter in a recombinant AAV would permit autonomous viral replication, but only in erythroid progenitor cells. In this report, we provide evidence that the B19p6 promoter is necessary and sufficient to impart autonomous replication competence and erythroid specificity to AAV in primary human **hematopoietic progenitor** cells. Thus, expression from the B19p6 promoter plays an important role in post-P-antigen receptor erythroid-cell specificity of **parvovirus B19**. The AAV-**B19** hybrid vector system may also prove to be useful in potential gene therapy of human hemoglobinopathies.

L22 ANSWER 13 OF 19 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95153922 EMBASE
DOCUMENT NUMBER: 1995153922
TITLE: [**Parvovirus B19** infection and pregnancy].
INFECTION A **PARVOVIRUS B19** ET GROSSESSE.
AUTHOR: Savey L.; Poissonnier M.-H.; Leblanc M.; Colau J.-C.
CORPORATE SOURCE: Service de Gynecologie-Obstetrique, CMC Foch, 40, rue Worth,F 92150 Suresnes, France
SOURCE: Journal de Gynecologie Obstetrique et Biologie de la Reproduction, (1995) 24/2 (170-176).
ISSN: 0368-2315 CODEN: JGOBAC
COUNTRY: France
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
010 Obstetrics and Gynecology
LANGUAGE: French
SUMMARY LANGUAGE: English; French
AB **Parvovirus B19** was identified in 1975. It causes infections megalerythemia in adults associated with skin eruptions and joint pain (about 50% of the adult population is immunized). The risk of contamination in case of an epidemia is high in school teachers and school personnel. In 1984, the **parvovirus B19** was implicated as the cause of fetal anasarca. The risk of transplacental contamination is estimated at 33% in case of maternal infection. Pregnant women with **parvovirus B19** infection and confirmed serology should have cut echography every 15 days. Fetal anasarca can be complicated by in utero fetal death related to erythroid stem-cell anaemia. The diagnosis of fetal infection is based on PCR techniques on fetal blood. Symptomatic antenatal treatment with in utero transfusion was proposed as early as 1988. This method does not however appear to be necessary in all cases as the outcome in severed reports of untreated fetuses was delivery of a normal child. There is the possibility of myocardial damage caused by **parvovirus B19** which would make in utero transfusion difficult and limit its beneficial effect. Finally associated thrombopenia is often severe and increased fetal risk.

L22 ANSWER 14 OF 19 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 94253728 MEDLINE
DOCUMENT NUMBER: 94253728 PubMed ID: 7515101
TITLE: Adeno-associated virus 2-mediated high efficiency gene transfer into immature and mature subsets of **hematopoietic progenitor** cells in human umbilical cord blood.
AUTHOR: Zhou S Z; Cooper S; Kang L Y; Ruggieri L; Heimfeld S; Srivastava A; Broxmeyer H E
CORPORATE SOURCE: Department of Medicine, Indiana University School of Medicine, Indianapolis 46202-5120.
CONTRACT NUMBER: R01 HL-48342 (NHLBI)
R29 AI-26323 (NIAID)
R37 CA-36464 (NCI)
+
SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, (1994 Jun 1) 179 (6) 1867-75.
Journal code: 2985109R. ISSN: 0022-1007.
PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199406
ENTRY DATE: Entered STN: 19940707
Last Updated on STN: 19970203
Entered Medline: 19940627

AB Recombinant adeno-associated virus 2 (AAV) virions were constructed containing a gene for resistance to neomycin (neoR), under the control of either the herpesvirus thymidine kinase (TK) gene promoter (vTK-Neo), or the human **parvovirus B19** p6 promoter (vB19-Neo), as well as those containing an upstream erythroid cell-specific enhancer (HS-2) from the locus control region of the human beta-globin gene cluster (vHS2-TK-Neo; vHS2-B19-Neo). These recombinant virions were used to infect either low density or highly enriched populations of CD34+ cells isolated from human umbilical cord blood. In clonogenic assays initiated with cells infected with the different recombinant AAV-Neo virions, equivalent high frequency transduction of the neoR gene into slow-cycling multipotential, erythroid, and granulocyte/macrophage (GM) progenitor cells, including those with high proliferative potential, was obtained without prestimulation with growth factors, indicating that these immature and mature **hematopoietic progenitor** cells were susceptible to infection by the recombinant AAV virions. Successful transduction did not require and was not enhanced by prestimulation of these cell populations with cytokines. The functional activity of the transduced neo gene was evident by the development of resistance to the drug G418, a neomycin analogue. Individual high and low proliferative colony-forming unit (CFU)-GM, burst-forming unit-erythroid, and CFU-granulocyte erythroid macrophage megakaryocyte colonies from mock-infected, or the recombinant virus-infected cultures were subjected to polymerase chain reaction analysis using a neo-specific synthetic oligonucleotide primer pair. A 276-bp DNA fragment that hybridized with a neo-specific DNA probe on Southern blots was only detected in those colonies cloned from the recombinant virus-infected cells, indicating stable integration of the transduced neo gene. These studies suggest that parvovirus-based vectors may prove to be a useful alternative to the more commonly used retroviral vectors for high efficiency gene transfer into slow or noncycling primitive **hematopoietic progenitor** cells, without the need for growth factor stimulation, which could potentially lead to differentiation of these cells before transplantation.

L22 ANSWER 15 OF 19 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 93100843 MEDLINE
DOCUMENT NUMBER: 93100843 PubMed ID: 8416383
TITLE: Successful replication of **parvovirus B19** in the human megakaryocytic leukemia cell line MB-02.
AUTHOR: Munshi N C; Zhou S; Woody M J; Morgan D A; Srivastava A
CORPORATE SOURCE: Department of Medicine, Indiana University School of Medicine, Indianapolis 46202-5120.
CONTRACT NUMBER: AI-26323 (NIAID)
HL-48342 (NHLBI)
SOURCE: JOURNAL OF VIROLOGY, (1993 Jan) 67 (1) 562-6.
Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199301

ENTRY DATE: Entered STN: 19930205
Last Updated on STN: 19970203
Entered Medline: 19930115

AB The pathogenic human **parvovirus B19** has been shown to undergo productive replication in the erythroid lineage in primary normal human **hematopoietic progenitor** cells. However, none of the established erythroleukemia cell lines has allowed B19 virus replication in vitro. The remarkable erythroid tissue tropism of B19 virus was evaluated with a human megakaryocytic leukemia cell line, MB-02, which is dependent on the growth factor granulocyte-macrophage colony-stimulating factor but can be induced to undergo erythroid differentiation following treatment with erythropoietin (Epo). Whereas these cells did not support B19 virus DNA replication in the presence of granulocyte-macrophage colony-stimulating factor alone, active viral DNA replication was observed if the cells were exposed to Epo for 5 to 10 days prior to B19 virus infection, as detected by the presence of the characteristic B19 virus DNA replicative intermediates on Southern blots. No replication occurred if the cells were treated with Epo for 3 days or less. In addition, complete expression of the B19 virus genome also occurred in Epo-treated MB-02 cells, as detected by Northern blot analysis. B19 progeny virions were released into culture supernatants that were biologically active in secondary infection of normal human bone marrow cells. The availability of the only homogeneous permanent cell line in which induction of erythroid differentiation leads to a permissive state for B19 virus replication in vitro promises to yield new and useful information on the molecular basis of the erythroid tissue tropism as well as **parvovirus B19**-induced pathogenesis.

L22 ANSWER 16 OF 19 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 92114159 MEDLINE
DOCUMENT NUMBER: 92114159 PubMed ID: 1731104
TITLE: Replication of **parvovirus B19** in **hematopoietic progenitor** cells generated in vitro from normal human peripheral blood.
AUTHOR: Schwarz T F; Serke S; Hottentrager B; von Brunn A; Baurmann H; Kirsch A; Stolz W; Huhn D; Deinhardt F; Roggendorf M
CORPORATE SOURCE: Max von Pettenkofer Institute for Hygiene and Medical Microbiology, Ludwig Maximilian University, Munich, Germany.
SOURCE: JOURNAL OF VIROLOGY, (1992 Feb) 66 (2) 1273-6.
Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199202
ENTRY DATE: Entered STN: 19920308
Last Updated on STN: 19970203
Entered Medline: 19920214

AB Erythroid progenitor cells generated in vitro from peripheral human blood in the presence of interleukin-3 and erythropoietin were infected with human **parvovirus B19**. **B19** virus DNA replication was highest 48 to 72 h after infection, and maximum levels of B19 virus proteins were detected in culture supernatants at 72 to 96 h after infection. B19 virus propagated in vitro was infectious. This cell culture system with peripheral blood cells facilitates studies in vitro of B19 virus replication.

L22 ANSWER 17 OF 19 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 92393245 MEDLINE
DOCUMENT NUMBER: 92393245 PubMed ID: 1520981
TITLE: Heat stability of **parvovirus B19**: kinetics of inactivation.
AUTHOR: Schwarz T F; Serke S; Von Brunn A; Hottentrager B; Huhn D; Deinhardt F; Roggendorf M
CORPORATE SOURCE: Max von Pettenkofer-Institut fur Hygiene und Medizinische Mikrobiologie, Ludwig-Maximilians-Universitat, Munchen, Germany.
SOURCE: ZENTRALBLATT FUR BAKTERIOLOGIE, (1992 Jul) 277 (2) 219-23. Journal code: 9203851. ISSN: 0934-8840.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199210
ENTRY DATE: Entered STN: 19921023
Last Updated on STN: 20000303
Entered Medline: 19921013

AB Heat inactivation of **parvovirus B19** (**B19**) was studied in a culture of **hematopoietic progenitor** cells generated in vitro from peripheral human blood. After inoculating cell cultures with identical volumes of plasma (MII) containing B19 (B19-MII) heat-treated (60 degrees C) for various periods of time, a time-dependent inactivation of the input virus was determined by a decrease of viral DNA replication. No B19 DNA was detected after infection with B19-MII heat-treated for 20 min or more by Southern blot. Viral B19 protein production decreased time-dependently and was not detected after infection with samples treated for 12 min at 60 degrees C or more determined by the enzyme immunoassay. This study indicates that infectivity of B19 virus in plasma can be reduced in vitro by heat-treatment (60 degrees C). However, this does not mean that the heat treatment completely inactivated B19 virus.

L22 ANSWER 18 OF 19 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 90123175 MEDLINE
DOCUMENT NUMBER: 90123175 PubMed ID: 2404522
TITLE: Susceptibility of human erythropoietic cells to **B19 parvovirus** in vitro increases with differentiation.
AUTHOR: Takahashi T; Ozawa K; Takahashi K; Asano S; Takaku F
CORPORATE SOURCE: Department of Hematology-Oncology, University of Tokyo, Japan.
SOURCE: BLOOD, (1990 Feb 1) 75 (3) 603-10. Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199003
ENTRY DATE: Entered STN: 19900328
Last Updated on STN: 19900328
Entered Medline: 19900314

AB **B19** human **parvovirus** is the etiologic agent of transient aplastic crisis. To better understand B19 virus-induced hematopoietic suppression, we studied the host cell range of the virus using in vitro bone marrow cultures. First, B19 virus replication was examined in the presence of various purified cytokines using DNA dot blot

analysis. Replication was detected only in erythropoietin-containing cultures. The other cytokines (granulocyte/macrophage colony-stimulating factor [GM-CSF], G-CSF, M-CSF, interleukin-1 [IL-1], IL-2, IL-3, and IL-6) did not support virus replication, indicating the restriction of B19 virus replication to the erythroid cell lineage. Second, **hematopoietic progenitor** cells were serially assayed in B19-infected and uninfected bone marrow cultures. At initiation, B19 virus infection caused marked and moderate reduction in colony-forming unit erythroid (CFU-E) and burst-forming unit erythroid (BFU-E) numbers, respectively, without affecting CFU-Mix and CFU-GM numbers. Interestingly, the recovery of the erythroid progenitor numbers was observed at a late stage of cultures despite the sustained reduction in erythroblasts. The cells in the bursts derived from such reappearing BFU-E did not contain the virus genome. Although infectious virus was detected in the culture supernatants, the cultured CFU-E harvested at day 5 was relatively resistant to B19 virus infection compared with the CFU-E in fresh bone marrow. These findings suggest that pluripotent stem cells escaped B19 virus infection and restored the erythroid progenitor cells later in infected cultures. We conclude that the target cells of B19 virus are in the erythroid lineage from BFU-E to erythroblasts, with susceptibility to the virus increasing along with differentiation. Furthermore, the suppression of erythropoiesis and the subsequent recovery of the erythroid progenitor numbers in B19-infected liquid cultures may be analogous in part to the clinical features of B19 virus-induced transient aplastic crisis.

L22 ANSWER 19 OF 19 MEDLINE DUPLICATE 11
ACCESSION NUMBER: 88275084 MEDLINE
DOCUMENT NUMBER: 88275084 PubMed ID: 3392774
TITLE: Replication of **B19 parvovirus** in highly enriched **hematopoietic progenitor** cells from normal human bone marrow.
AUTHOR: Srivastava A; Lu L
CORPORATE SOURCE: Department of Medicine, Indiana University School of Medicine, Indianapolis 46223.
SOURCE: JOURNAL OF VIROLOGY, (1988 Aug) 62 (8) 3059-63.
Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198808
ENTRY DATE: Entered STN: 19900308
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AB The target cell specificity of the **B19 parvovirus** infection was examined by isolating highly enriched **hematopoietic progenitor** and stem cells from normal human bone marrow. The efficiency of the **B19 parvovirus** replication in enriched erythroid progenitor cells was approximately 100-fold greater than that in unseparated bone marrow cells. The more-primitive progenitor cells identical to or closely related to the human pluripotent hematopoietic stem cells, on the other hand, did not support viral replication. The B19 progeny virus produced by the enriched erythroid progenitor cells was infectious and strongly suppressed erythropoiesis in vitro. The susceptibility of both the more-primitive erythroid progenitors (burst-forming units-erythroid) and the more-mature erythroid progenitors (CFU-erythroid) to the cytolytic response of the virus and the lack of effect on the myeloid progenitors (CFU-granulocyte-macrophage) further

give evidence to the remarkable tropism of the **B19 parvovirus** for human hematopoietic cells of erythroid lineage.